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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/254,529	08/04/1999	SUSAN MARY KINGSMAN	9192.9USWO	7151

7590 11/26/2004

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EXAMINER	
KAUSHAL, SUMESH	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 11/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/254,529	KINGSMAN ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1636	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 12 October 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires *4* months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *28-30,33,34,36-38 and 40-43*.

   Claim(s) withdrawn from consideration: _____.

8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

JEFFREY FREDMAN
PRIMARY EXAMINER
1/6/1

Continuation of 3. Applicant's reply has overcome the following rejection(s): Written description and enablement rejection under 35 USC 112(1) regarding claim 37..

Continuation of 5. does NOT place the application in condition for allowance because: Claims 28-30, 33-34, 36-38 and 40-43 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Lisziewicz (WO92/21750, 1992, ref of record), Hope et al (PNAS, 87:7787-7791, 1990, ref of record) and Riviere et al (US 6544771, 2003) for the same reasons of record as set forth in the office action mailed on 06/10/04.

RESPONSE TO ARGUMENT

The applicant argues that there is no teaching in any of the references that renders the claimed invention obvious. Lisziewicz, Hope or Riviere, alone or in combination, do not teach a Tat- and Rev inducible retroviral vector, where there is no basal transcription in the absence of Tat and Rev. The applicant argues that on the other hand, the claimed invention achieves a Rev-dependent intron by the placement of splice sites that flank an RRE-containing intron, and by the splice sites being derived from different retroviruses. The applicant argues that neither Lisziewicz, Hope or Riviere teach, suggest or provide a motivation to make a retroviral vector having splice sites derived from a different retrovirus.

However, applicant's arguments are found NOT persuasive. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine, 837 F.2d 1071, 5 USPQ2 1596 (Fed. Cir. 1988) and In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). The rationale to modify or combine the prior art does not have to be expressly stated in the prior art; the rationale may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art, established scientific principles, or legal precedent established by prior case law (See MPEP 2144).

In this case, Liziewicz teaches a retroviral vector (MLV) incorporating HIV Rev/RRE system, wherein the RRE is located within the transcriptional unit of the foreign gene or within the transcriptional unit of the vector. The retroviral vector (MLV) as taught by Liziewicz include a strong promoter (HIV LTR) which is switched on in the presence of the virus or viral-transactivator protein (tat), but in the absence of viral infection does not express the encoded gene product. Therefore, Liziewicz clearly teaches a retroviral vector wherein the nucleotide sequence of interest is located within an intron in the transcription unit of a provirus and the gene expression is only limited to HIV infected cells in the presence of tat.

Hope teaches a retroviral vector comprising splice donor sequence, RRE and splice acceptor sequences, wherein the gene of interest (CAT) is located within the splice donor and splice acceptor sites (page 7787, abstract; page 7788, fig-1). The transcripts produced by this vector harbor a single intron, which contain CAT coding sequences (page 778, col.1. Para.1).

Even though the combined teaching of Liziewicz and Hope suggest a tat/rev responsive retroviral vector the cited does not teach splice donor (SD) and splice acceptor (SA) sites derived from different retroviral vectors that flanks the provirus intron and gene of interes

Riviere teaches a recombinant retroviral vector containing splice donor and splice acceptor cites obtained from different retroviruses comprising: (i) a 5' LTR derived from a retrovirus of interest; (ii) a splice donor site located 3' to said 5' LTR; (iii) a Psi packaging site located 3' to said splice donor site; (iv) a consensus splice acceptor site, located 3' to said Psi packaging site; (v) an insertion site for a gene of interest located 3' to said consensus splice acceptor site; and (vi) a 3' LTR derived from a retrovirus of interest located 3' to said insertion site (Col. 28, lines 44-57; Col. 29, lines 15-30, Col. 30 lines 50-65).

Thus it would have been obvious to one ordinary skill in the art at the time of filing to modify the retroviral vector (MLV) as taught by Liziewicz, by incorporating a nucleotides of interest within the splice acceptor site (HIV) as taught by Hope. One would have been motivated to do so because the insertion of a RRE (HIV) into the intron of foreign gene and within splice donor and splice acceptor sites provides the regulation of the expression of a foreign gene by RRE element which is only switched on in the presence REV protein. It would have been further obvious to modify the combined teaching of Liziewicz and Hope by substituting splice donor and splice acceptor sites derived from different retroviruses. One would have been motivated to incorporate HIV splice acceptor site to conserve the functionally of HIV RRE in the construct. One would have a reasonable expectation of success because the regulation of HIV LTR by Tat protein and RRE by Rev-protein has been a well characterize phenomenon in the art at the time the instant invention was made. In addition making a retroviral vector containing splice donor and splice acceptor sites derived from different retroviruses is well within the reach of one ordinary skill in the art, since art at the time of filing clearly teaches that even consensus sequence comprising a splice dono and splice acceptor sites are capable of producing spliced transcripts. Thus the invention as claimed is prima facie obvious in view of the prior art of record..